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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,748	02/27/2001	Adi Kimchi	KIMCHI 2A	4171

1444 7590 06/13/2002

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EXAMINER
MONSHIPOURI, MARYAM

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/13/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/719,748	Kimchi et al.
Examiner	**Art Unit**
Maryam Monshipouri	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20, 23, 24, and 26-30* is/are pending in the application.

4a) Of the above, claim(s) *2-7, 9-12, 14-19, 23, 24, 26, 29, and 30* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 8, 13, 20, 27, and 28* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's response to restriction requirement filed 5/6/2002 (Paper # 11) is acknowledged. Applicant elected Group I invention directed to claims 1, 8, 12, 20, 27 and 28 with traverse. Claims 2-7, 9-12, 14-19, 23-24, 26 and 29-30 are withdrawn as drawn to non-elected invention. Claims 21-22 and 25 have been canceled.

In traversal of lack of unity requirement applicant argues that according to PCT administrative instructions, Annex B, Unity of Invention, Part 2, Example 17, protein X and DNA encoding it have unity of invention and thus lack of unity held between Inventions of Group I and II should be withdrawn.

This argument was fully considered but was found **unpersuasive**. This is because Inbal et al. (SPTREMBL Database, Accession No. O75892, 11/1998, which teaches a cell inducing polypeptide having 99.2% identity to SEQ ID NO:2 of this invention) is anticipatory to polypeptide of Group I (see claim sections 1(B) and 1(D)). Thus, even though DNA sequences and polypeptides may in some cases share a common technical feature according to PCT administrative instructions, Annex B, Unity of Invention, Part 2, Example 17, said fact is not relevant to this case because the polypeptides of this case cannot be considered to be a special technical feature of Group I and Group II inventions under PCT rule 13.2. Hence, lack of unity of invention is maintained, as explained in the previous office action, and is hereby made **Final.**

DETAILED ACTION

Claims 1, 8, 12, 20, 27 and 28 are under examination on the merits.

Claim Objections

1. Claim 1 and 20 are objected to because of the following informalities: in claim 1(B) The term "property being" is confusing. Applicant is advised top insert the term. "of" between "property" and "being". Appropriate correction is required.

2. ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8, 13, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides consisting of amino acid residues 13-275 of SEQ ID NO:2 or consisting or residues 321-360 of SEQ ID NO:2, does not reasonably provide enablement for polypeptides **comprising** an amino acid sequence having 85% sequence identity to residues 13-275 or residues 321-360 of SEQ ID NO:2 wherein said polypeptides have no specific function.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The disclosure does not teach which residues among residues 13-275 of SEQ ID NO:2 are in charge of assigning function to said fragment. No examples of such residues are provided either. Current state of prior art indicates that any polypeptide variant which retains 85% or more identity to said fragment of SEQ ID NO:2 is not necessarily retaining kinase activity.

Therefore due to lack of sufficient examples and information provide in the disclosure and due to unpredictability of prior art as to structural requirements of polypeptide variants, which have at least 85% identity to residues 13-275 of SEQ ID NO:2, and retain kinase activity one of skill in the art has to go through the burden of undue experimentation in order to prepare the claimed polypeptides and as such claim 8 goes beyond the scope of the disclosure. Since claim 8 polypeptides are not enabled compositions comprising said polypeptides (claim 27) are not enabled either.

With respect to claim 13, residues 321-360 of SEQ ID NO:2 provide very little structural information about the claimed polypeptides. The disclosure once again fails to teach which residues within such small fragment of SEQ ID NO:2 are in charge of preventing for DRP-1 dimerization resulting in functionality of the kinase domain. Current state of prior art indicates that any sequence which happens to retain 85% identity to residues 321-360 of SEQ ID NO:2 is not capable of preventing DRP-1 dimerization.

Thus, due to lack of sufficient guidance and examples in the specification and due to unpredictability of prior art as to which variants of residues 321-360 of SEQ ID NO:1 and likely to prevent DRP-1 dimerization one of skill in the art has to go through the burden of undue

experimentation in order to prepare the claimed polypeptides and as such the claim goes beyond the scope of he disclosure. Since claim 13 is not enabled, composition comprising said sequence also lack enablement.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 20 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Polypeptide of claims 1(E) and 1(F) are confusing because even though said polypeptide as claimed must lack the cell-death domain (see page 5 of the specification) they must inhibit kinase activity which is disclosed to be only due to the action of cell-death domain. Thus, it is not clear how claimed polypeptides can simultaneously retain both functions recited. Claims 20 and 27 are merely rejected for depending on the rejected base claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1, 8, 20 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Deiss et al. (Genes dev., 9, 15-30, 1995, cited in the IDS). Deiss teaches a DAP kinase which has 83.7% identity to residues 13-275 of SEQ ID NO:2 (see the attached alignment) prior to this invention which is capable of inducing cell death. Since sequence alignment results change upon changing analysis parameters and 83.7% is very close to 85%, it is reasonable to deduce that Deiss's sequence has 85% identity to residues 13-275 of SEQ ID NO:2 of this invention, anticipating claim 1(D), 8. Further Deiss teaches preparation of a cell lysate comprising recombinant DAP kinase (see page 28, column 1) said lysate can be considered to be a composition comprising a polypeptide comprising residues 13-275 of SEQ ID NO:2, anticipating claims 20 and 27.

8. Claims 1, 8, 20 and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Akira et al., (EP 911408, Apr 1999). Akira teaches a murine Zip kinase that has 82.4% identity to residues 13-275 of SEQ ID NO:2 and can indue cell death. Since sequence alignment results change upon changing analysis parameters and 82.4% is very close to 85%, it is reasonable to deduce that Akira's sequence has 85% identity to residues 13-275 of SEQ ID NO:2 of this invention, anticipating claim 1(D), 8. Akira teaches isolation of recombinant murine Zip kinase (see page 5) from transformant culture broth, wherein said broth or even said transformant can be considered to be compositions comprising said kinase anticipating claims 20 and 27.

9. Claims 1 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Inbal et al. (cited above). Inbal teaches a polypeptide sequence which is capable of inducing cell death and

has 99.4% identity to SEQ ID NO:2 of this invention (see the attached alignment) anticipating claim 1(B) and 8.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Inbal (cited above) in view of Kimchi (WO 95/10630, Apr 1995, cited in the IDS) further in view of Kawai et al. (Mol. Cell. Biol., 18, 1642-1651, 1998). Inbal, as stated above, teaches a polypeptide that has 99.4% homology to SEQ ID NO:2 of this invention. Inbal does not teach a polypeptide consisting of amino acid residues 321-360 of SEQ ID NO:2 or 85% or more homologs thereof, corresponding to cell-death domain of this protein.

Kawai teaches that cell-death domain of ZIP kinase, a family member of apoptosis inducing kinases such as DRP-1 of this invention, corresponding to last 40-50 residues of human and mouse ZIP kinases (see residues 408-445 in mouse polypeptide and residues 413-450 , corresponding to 37 amino acids, in human ZIP kinases, indicated at page 1643 of Kawai et al.), respectively, is located at its carboxy treminus. Similarly, Kimchi teaches that the last 47 amino acids of DAP kinase, another member of apoptosis inducing kinases and most similar to DRP-1 of this invention, can be cleaved from the protein body due to post-transnational modifications.

Considering the state of structural information with respect to apoptosis inducing kinases in the prior art, it would have been obvious to one of ordinary skill in the art to start with the polypeptide of Inbal and cleave its carboxy terminal corresponding to last 40-50 residues of said sequence, with the expectation of obtaining the cell-death domain of said protein. Such fragment would at least have 85% identity to residues 320-361 of SEQ ID NO:2 of this invention. One of ordinary skill in the art is motivated to cleave the last 40-50 residues of Inbal, at its carboxy terminus because, firstly, the truncated DRP-1, similar to DAP kinase, lacking the cell-death domain can no longer homodimerize and thereby induce apoptosis and, secondly, obtaining antibodies which specifically bind said cleaved cell-death domain may be useful in detecting other cell-death inducing proteins in vivo. Thus, both products obtained by such cleavage are of great interest to one of ordinary skill in the art.

One of ordinary skill in the art has a reasonable expectation of success in cleaving the last 40-50 maino acids of Inbal's sequence at its carboxy terminal because methods of cleaving polypeptides are merely routine in the prior art and Kimchi already has indicated that in naturally produced DAP kinase a homolog of DRP-1, such carboxy fragments are cleaved in the cell due to post-transnational modification, rendering the invention obvious.

No claim are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Maryam Monshipouri, Ph.D. whose telephone number is (703) 308- 1083.

The Examiner can normally be reached daily from 8:30 A.M. to 4:00 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. P. Achutamurthy, can be reached at (703) 308-3804. The OFFICIAL fax number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

M. Monshi

Maryam Monshipouri, Ph.D.

Patent Examiner